Claims

1. A method for increasing the systemic exposure of cells selected from tumor cells and normal cells to an orally administered pharmaceutically active compound, wherein a bioenhancer comprising an inhibitor of BCRP is orally administered concomitantly with said orally administered pharmaceutically active compound.
2. Method according to claim 1, wherein the inhibitor is administered simultaneously with the pharmaceutical compound.
3. Method according to claim 1 or claim 2, wherein the cells are normal cells.
4. Method according to any of the preceding claims, wherein the inhibitor is a selective inhibitor of BCRP.
5. Method according to any of the preceding claims, wherein the inhibitor is selected from acridine derivatives, quinoline derivatives, isoquinoline derivatives and combinations thereof.
6. Method according to any of the preceding claims, wherein the inhibitor is GF120918, XR 9051 or XR 9576.
7. Method according to any of the preceding claims, wherein the bioenhancer is a mycotoxin.
8. Method according to claim 7, wherein the mycotoxin is fumitremorgin C.
9. Method according to any of the preceding claims, wherein the bioenhancer has a higher affinity for BCRP than for P-gp.
10. Method according to any of the preceding claims, wherein the bioenhancer has a higher affinity for BCRP than for MRP.
11. Method according to any one of the preceding claims, wherein the bioenhancer inhibits binding of ATP to a BCRP mediated and/or related drug transport protein.
12. Method according to claim 11, wherein the protein is BCRP.
13. Method according to any of the preceding claims, wherein the pharmaceutically active compound is selected from the group consisting of indolizino-quinoline derivatives, camptothecin derivatives, anthraquinone derivatives and quinazoline derivatives.
14. Method according to claim 13, wherein the pharmaceutically active compound is an indolizino-quinoline derivative.

15. Method according to claim 13, wherein the pharmaceutically active compound is a camptothecin derivative.

16. Method according to claim 15, wherein the pharmaceutically active compound is selected from the group consisting of topotecan, GG211, DX8951f, BNP1350, 9-aminocamptothecin, 9-nitrocamptothecin, CPT11 and any metabolites thereof.

17. Method according to claim 16, wherein the metabolite is SN38.

18. Method according to claim 13, wherein the pharmaceutically active compound is an anthraquinone derivative.

19. Method according to claim 18, wherein the pharmaceutically active compound is mitoxantrone.

20. Method according to claim 13, wherein the pharmaceutically active compound is a quinazoline derivative.

21. Method according to claim 20, wherein the pharmaceutically active compound is prazosin.

22. Pharmaceutical composition comprising a bioenhancer and a pharmaceutically active compound, said bioenhancer comprising an inhibitor of BCRP and said pharmaceutically active compound being selected from the group consisting of indolizino-quinoline derivatives, camptothecin derivatives, anthraquinone derivatives and quinazoline derivatives.

23. Use of a pharmaceutically active compound in combination with a bioenhancer as defined in any of the preceding claims as active ingredients in the preparation of a pharmaceutical composition for oral delivery of the pharmaceutically active compound, said pharmaceutical composition providing an increased systemic exposure of cells selected from tumor cells and normal cells to said pharmaceutically active compound in comparison to a corresponding pharmaceutical composition in which said bioenhancer is absent.

24. Use of a pharmaceutically active compound in combination with a bioenhancer as defined in any of the preceding claims as active ingredients in the preparation of a pharmaceutical composition for oral delivery of the pharmaceutically active compound, said pharmaceutical composition providing an increased reversal of drug resistance in human and animal disorders related to overexpression of BCRP.

25. Animal having inactive BCRP and/or being free of BCRP.

26. A method of screening for a compound useful for increasing bioavailability of an orally administered drug in a mammal, said drug being transported via the BCRP related or mediated drug transport system by assaying a candidate compound for inhibition of transport by BCRP and selecting a compound exhibiting such inhibition, in particular exhibiting such inhibition in the gut or gastrointestinal tract.

27. Use of a compound selected according to claim 26 as bioenhancer in a pharmaceutical composition according to claim 22.

28. Use of a monoclonal antibody specific for a BCRP, preferably a human BCRP, as bioenhancer in a pharmaceutical composition according to claim 22.

29. Use of an animal according to claim 25 for screening for a compound useful for increasing bioavailability of an orally administered drug in a mammal, said drug being transported via the BCRP related and/or mediated drug transport system by assaying a candidate compound for inhibition of transport by BCRP and selecting a compound exhibiting such inhibition, in particular exhibiting such inhibition in the gut or gastrointestinal tract.

Patent Specification